CLAIMS

We claim:

1. A method for detecting the presence of a reproductive function-modulating organism, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome.

2. The method of claim 1, wherein the correlation with at least one of the presence and risk of the condition is made if the organism is capable of remaining adherent to sperm after washing a sample comprising organism-positive sperm to permit at least one of removal and separation of non-sperm substances from the sample.

3. The method of claim 1, wherein the correlation with at least one of the presence and risk of the condition is made if the washed sperm sample comprises at least 0.01% of the total number of organisms present in the sperm sample before washing.

4. The method of claim 1, wherein the washing is carried out using wash conditions that protect one or more viability properties of the sperm.

5. The method of claim 4, wherein the wash conditions are characterized in that they permit the continuation of adherence of *Ureaplasma parvum* serotype 6 to the sperm but do not permit the continuation of adherence of *U. parvum* serotype 1 to the sperm.

6. The method of claim 1, wherein the washing is carried out using a sperm swim-up technique.

7. The method of claim 1, wherein the washing is carried out using gradient centrifugation.

8. The method of claim 1, wherein the organism is selected from the class Mollicutes.

9. The method of claim 1, wherein the organism is selected from the order Mycoplasmatales.

10. The method of claim 1, wherein the organism is selected from the family Mycoplasmataceae.

11. The method of claim 1, wherein the organism is an ureaplasma.

12. The method of claim 1, wherein the organism is selected from the genus *Ureaplasma*.

13. The method of claim 12, wherein the organism is selected from the group consisting of a subtype of a strain and serotype selected from the group consisting of *Ureaplasma parvum* and *Ureaplasma urealyticum*.

14. The method of claim 12, wherein the organism is a subtype of *Ureaplasma parvum* serotype 6.

15. The method of claim 1, wherein the organism is selected from the genus *Mycoplasma*.

16. The method of claim 15, wherein the organism is selected from the group consisting of a subtype of a strain or serotype of *Mycoplasma hominis*.

17. The method of claim 1, wherein the adverse pregnancy outcome is selected from the group consisting of miscarriage, pre-term delivery, premature onset of labor, prolonged rupture of membranes, neonatal morbidity and mortality.

18. The method of claim 1, wherein the adverse ART outcome is selected from the group consisting of reduced embryonic development, reduced implantation rate, reduced fertilization rate, reduced clinical pregnancy rate, reduced viable pregnancy rate, reduced blastocyst culture rate and increased miscarriage rate.

19. A method for detecting the presence of a reproductive function-modulating organism, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility.

20. A method for detecting the presence of a reproductive function-modulating organism, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse pregnancy outcome.

21. A method for detecting the presence of a reproductive function-modulating organism, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse assisted reproductive technology (ART) outcome.

22. A method for detecting an organism associated with at least one of male infertility and an increased risk of male infertility, comprising detecting an organism which is capable of

adhering to sperm and which correlates with at least one of a presence and the risk of male infertility.

23. A method for detecting an organism associated with at least one of an adverse pregnancy outcome and an increased risk of an adverse pregnancy outcome, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and the risk of the adverse pregnancy outcome.

24. A method for detecting an organism associated with at least one of an adverse assisted reproductive technology (ART) outcome and an increased risk of an adverse ART outcome, comprising detecting an organism which is capable of adhering to sperm and which correlates with at least one of a presence and the risk of the adverse ART outcome.

25. A method for detecting at least one of a presence and diagnosing the risk of infertility in a male patient, comprising detecting in a sperm sample obtained from the patient an organism which is capable of adhering to sperm and which correlates with at least one of the presence and the risk of male infertility.

26. A method for detecting at least one of a presence and diagnosing the risk of an adverse pregnancy outcome in a patient, comprising detecting an organism in a sperm sample obtained from a sperm donor of the patient, wherein the organism is capable of adhering to sperm and correlates with at least one of the presence and the risk of an adverse pregnancy outcome.

27. A method for detecting at least one of a presence and diagnosing the risk of an adverse assisted reproductive technology (ART) outcome, comprising detecting the presence of an organism in a sperm sample used for the ART, wherein the organism is capable of adhering to sperm and correlates with at least one of the presence and the risk of an adverse ART outcome.

28. The method of claim 27, wherein the ART is selected from the group consisting of artificial insemination (AI), *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI).

29. A method for detecting at least one of a presence of and diagnosing a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome in a patient, comprising detecting an organism in a biological sample obtained from the patient, wherein the organism is capable of adhering to sperm and correlates with at least one of the presence and the risk of the condition.

30. The method of claim 29, wherein the biological sample comprises a biological fluid selected from the group consisting of whole blood, serum, plasma, saliva, urine, sweat, ascitic fluid, peritoneal fluid, synovial fluid, cerebrospinal fluid, amniotic fluid, seminiferous tubule fluid, semen, vaginal secretions, endocervical secretions, respiratory secretions, endometrial lining, fallopian tube washings, and follicular fluid.

31. The method of claim 29, wherein the biological sample comprises a tissue biopsy of at least one tissue selected from the group consisting of spermatozoan, endocervical cell, placental tissue, endometrial biopsy, chorioamnion, seminiferous tubule, ovarian tissue, oocyte, embryo, single cells biopsied from embryo, and fallopian tube tissue.

32. A method for diagnosing a higher risk of infertility in a male patient, comprising detecting in a biological sample obtained from the patient an organism which is capable of adhering to sperm and which correlates with a higher risk of male infertility.

33. A method for diagnosis of a higher risk of an adverse pregnancy outcome in a patient, comprising detecting an ureaplasma in a biological sample obtained from a sperm donor of the patient, wherein the organism is capable of adhering to sperm and correlates with a higher risk of an adverse pregnancy outcome.

34. A method for diagnosis of a higher risk of an adverse assisted reproductive technology (ART) outcome using sperm of a patient, comprising detecting an organism in a biological sample obtained from the patient, wherein the organism is capable of adhering to sperm and correlates with a higher risk of an adverse ART outcome.

35. An isolated adhesin, wherein the adhesin is obtainable from an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome.

36. The adhesin of claim 35, which is capable of binding to a carbohydrate moiety on the surface of the sperm.

37. The adhesin of claim 35, which is capable of binding to a glycolipid.

38. The adhesin of claim 37, which is capable of binding to sulfogalactosylceramide.

39. The adhesin of claim 37, which is capable of binding to sulfatoxygalactosylceramide.

40. An isolated polynucleotide encoding the adhesin of claim 39.

41. A method for detecting an organism associated with at least one of male infertility and with an increased risk of male infertility, comprising interrogating a microbial sample for the presence of a gene encoding at least one of an adhesin and an expression product of the gene, wherein the adhesin is expressed by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility.

42. A method for detecting an organism associated with at least one of male infertility and an increased risk of male infertility, comprising interrogating a microbial sample for the presence of at least one of a gene encoding an adhesin and an expression product of the gene, wherein the at least one of the adhesin and the expression product is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility.

43. A method for detecting an ureaplasma associated with at least one of an adverse pregnancy outcome and an increased risk of an adverse pregnancy outcome, comprising interrogating a microbial sample for at least one of a presence of a gene encoding an adhesin and an expression product of the gene, wherein at least one of the adhesin and the expression product is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of the presence and risk of the adverse pregnancy outcome.

44. A method for detecting an ureaplasma associated with at least one of an adverse assisted reproductive technology (ART) outcome and an increased risk of an adverse ART outcome, comprising interrogating a microbial sample for a presence of at least one of a gene encoding an adhesin and an expression product of the gene, wherein at least one of the adhesin and the expression product is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of the adverse ART outcome.

45. A method of screening for an agent which modulates the adherence of an organism to spermatozoa, wherein the organism is capable of adhering to sperm and correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome, the method comprising:

(a) contacting with a test agent a preparation comprising at least one of:

(i) a polypeptide comprising an amino acid sequence corresponding to at least a biologically active fragment of the adhesin of claim 35, and

(ii) a polynucleotide comprising at least a portion of a genetic sequence that regulates the expression of the adhesin of claim 35 and that is operably linked to a reporter gene; and

(b) detecting a change in at least one of a level and functional activity of at least one of the polypeptide and an expression product of the reporter gene, relative to at least one of a reference level and functional activity in the absence of the test agent.

46. A method of using an adhesin to produce an antigen-binding molecule that is immuno-interactive with the adhesin, wherein the adhesin is obtainable from an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome.

47. An antigen-binding molecule produced by the method of claim 46.

48. An antigen-binding molecule that is immuno-interactive with an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome.

49. A method of detecting an adhesin in a biological sample, wherein the adhesin is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome, the method comprising:

contacting the sample with the antigen-binding molecule of claim 48; and

detecting the presence of a complex comprising the antigen-binding molecule and the adhesin in the contacted sample.

50. A method for prognostic assessment of at least one of male infertility, adverse pregnancy outcome and adverse assisted reproductive technology (ART) outcome in a patient, comprising detecting in a biological sample obtained from the patient a gene encoding at least one of an adhesin and an expression product of the gene, wherein the adhesin is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome.

51. A method for affecting an adhesin selected from the group consisting of masking an adhesin and for otherwise interfering with the binding of the adhesin to sperm, wherein the adhesin is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome, the method comprising contacting the adhesin with an antigen-binding molecule that is immuno-interactive with the adhesin.

52. A method for modulating adherence of an organism to sperm, wherein the organism is capable of adhering to sperm and correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome, the method comprising contacting the organism with an agent that modulates the adherence of the organism to spermatoza, wherein the agent is identified by the method of claim 45.

53. The method of claim 52, wherein the agent decreases at least one of the level and functional activity of the adhesin.

54. A composition for improving male fertility, comprising an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility, and optionally a pharmaceutically acceptable carrier.

55. A composition for enhancing propensity for a favorable pregnancy outcome, comprising an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse pregnancy outcome, and optionally a pharmaceutically acceptable carrier.

56. A composition for enhancing propensity for a favorable assisted reproductive technology (ART) outcome, comprising an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse ART outcome, and optionally a pharmaceutically acceptable carrier.

57. A method for at least one of a treatment and prophylaxis of male infertility, comprising administering to a patient in need of such treatment an effective amount of an agent that

reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility, optionally in the presence of a pharmaceutically acceptable carrier.

58. The method of claim 57, wherein the agent is at least one of an antisense oligonucleotide and a ribozyme that interacts specifically with a polynucleotide encoding at least one of the adhesin and complement thereof.

59. The method of claim 57, wherein the agent is an antigen-binding molecule that is immuno-interactive with the adhesin.

60. A method for at least one of a treatment and prophylaxis of male infertility, comprising administering to the sperm of a patient in need of such treatment an effective amount of an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of male infertility, optionally in the presence of a pharmaceutically acceptable carrier.

61. The method of claim 60, wherein the agent is at least one of an antisense oligonucleotide and a ribozyme that interacts specifically with a polynucleotide encoding at least one of the adhesin or complement thereof.

62. The method of claim 60, wherein the agent is an antigen-binding molecule that is immuno-interactive with the adhesin.

63. A method for enhancing propensity for a favorable pregnancy outcome in a patient, comprising administering to a sperm donor of the patient an effective amount of an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse pregnancy outcome, optionally in the presence of a pharmaceutically acceptable carrier.

64. The method of claim 63, wherein the agent is at least one of an antisense oligonucleotide and a ribozyme that interacts specifically with a polynucleotide encoding at least one of the adhesin and complement thereof.

65. The method of claim 63, wherein the agent is an antigen-binding molecule that is immuno-interactive with the adhesin.

66. A method for enhancing propensity for a favorable pregnancy outcome in a patient, comprising administering to the sperm of the patient's sperm donor an effective amount of an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse pregnancy outcome, optionally in the presence of a pharmaceutically acceptable carrier.

67. A method for enhancing propensity for a favorable assisted reproductive technology (ART) outcome in a patient, comprising administering to the sperm of the patient's sperm donor an effective amount of an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence or risk of an adverse ART outcome, optionally in the presence of a pharmaceutically acceptable carrier.

68. The method of claim 66, wherein the agent is at least one of an antisense oligonucleotide and a ribozyme that interacts specifically with a polynucleotide encoding at least one of the adhesin and complement thereof.

69. The method of claim 66, wherein the agent is an antigen-binding molecule that is immuno-interactive with the adhesin.

70. A method for enhancing propensity for a favorable assisted reproductive technology (ART) outcome in a patient, comprising administering to the sperm of the patient's sperm donor an effective amount of an agent that reduces at least one of a level and functional activity of an adhesin that is expressible by an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of an adverse ART outcome.

71. The method of claim 70, wherein the agent is at least one of an antisense oligonucleotide and a ribozyme that interacts specifically with a polynucleotide encoding at least one of the adhesin and complement thereof.

72. The method of claim 70, wherein the agent is an antigen-binding molecule that is immuno-interactive with the adhesin.

73. An immunopotentiating composition for eliciting production of an element that specifically binds to an organism which is capable of adhering to sperm and which correlates with at least one of a presence and risk of a condition selected from the group consisting of male infertility, an adverse pregnancy outcome and an adverse assisted reproductive technology (ART) outcome, the

composition comprising at least one of a proteinaceous molecule that is an isolated adhesin of the organism and a vector including a polynucleotide encoding the proteinaceous molecule and operably linked to a regulatory polynucleotide, wherein the composition optionally further comprises a pharmaceutically acceptable carrier or adjuvant.

74. A method for at least one of a treatment and prophylaxis of male infertility, comprising administering to a patient in need of such treatment an immunogenically effective amount of the immunopotentiating composition of claim 73.

75. A method for at least one of a treatment and prophylaxis of an adverse pregnancy outcome in a patient, comprising administering to the patient's sperm donor an immunogenically effective amount of the immunopotentiating composition of claim 73.

76. A method for at least one of a treatment and prophylaxis of an adverse assisted reproductive technology (ART) outcome in a patient, comprising administering to the patient's sperm donor an immunogenically effective amount of the immunopotentiating composition of claim 73.